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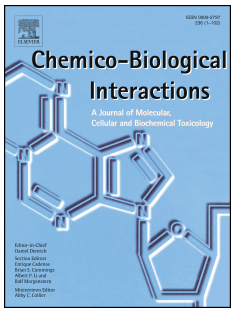

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Synergistic and additive effects of ATRA in combination with different anti-tumor compounds

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Abstract

All-trans retinoic acid (ATRA), a derivative of vitamin A, has been shown to potentiate cancer chemotherapy due to its ability to induce signals for cell differentiation or death, and inhibit cell proliferation. The combination of ATRA with taxoids, kinase inhibitors, natural compounds, retinoids, ER or HER2 inhibitors, chemotherapeutic drugs, proteasome inhibitors and nanoformulations of tretinoin have demonstrated additive or synergistic effects in anti-cancer activities. The mechanisms by which the compounds exert their synergistic effects depend on the tumor and the cell type. However, several experiments demonstrated similar mechanisms such as reduction of PCK, c-myc, E2F and Bcl-2, as well as increase of p21 and TGF-β. When the apoptotic synergistic effect was observed, the predominant effect of ATRA was in differentiation induction. The results indicate that future combinations of ATRA and anti-tumor agents hold promise to enhance and improve anti-carcinogenic therapies.

Key words: retinoic acid, cancer, anti-tumor